



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>7</sup> :</b> <b>C12N 15/12, 15/62, C07K 14/47, 16/18,</b> <b>C12Q 1/68, G01N 33/53</b>	<b>A3</b>	<b>(11) International Publication Number:</b> <b>WO 00/22130</b> <b>(43) International Publication Date:</b> 20 April 2000 (20.04.00)
<b>(21) International Application Number:</b> PCT/US99/24222 <b>(22) International Filing Date:</b> 14 October 1999 (14.10.99)  <b>(30) Priority Data:</b> 60/104,351 15 October 1998 (15.10.98) US Not furnished 13 October 1999 (13.10.99) US  <b>(71) Applicant:</b> CHIRON CORPORATION [US/US]; 4560 Horton Street, Emeryville, CA 94608 (US).  <b>(72) Inventor:</b> GIESE, Klaus; Atugen Biotechnology GmbH, Robert-Rossie-Strasse 10, D-13125 Berlin (DE).  <b>(74) Agents:</b> POTTER, Jane, E., R.; Seed and Berry LLP, 6300 Columbia, 701 Fifth Avenue, Seattle, WA 98104-7092 (US) et al.		<b>(81) Designated States:</b> AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).  <b>Published</b> <i>With international search report.</i>  <b>(88) Date of publication of the international search report:</b> 5 October 2000 (05.10.00)
<b>(54) Title:</b> METASTATIC BREAST AND COLON CANCER REGULATED GENES		
<b>(57) Abstract</b>		
<p>Gene sequences as shown in SEQ ID NOS:1-85 have been found to be significantly associated with metastatic potential of cancer cells, especially breast and colon cancer cells. Methods are provided for determining the risk of metastasis of a tumor, which involve determining whether a tissue sample from a tumor expresses a polypeptide encoded by a gene as shown in SEQ ID NOS:1-85, or a substantial portion thereof.</p>		

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## INTERNATIONAL SEARCH REPORT

Internat Application No

PCT/US 99/24222

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C12N15/62 C07K14/47 C07K16/18 C12Q1/68  
G01N33/53

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C12N C12Q G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>DATABASE EMSTS [Online] E.M.B.L. Databases Accession Number: G21051, 1 June 1996 (1996-06-01) HUDSON T: "Human STS WI-12648, sequence tagged site" XP002134106 96.3% identity in 134 bp overlap with SeqIdNo.1 abstract</p> <p>---</p> <p>SCOTLANDI K ET AL: "Multidrug resistance and malignancy in human osteosarcoma" CANCER RES, vol. 56, no. 10, 15 May 1996 (1996-05-15), pages 2434-2439, XP002134105</p> <p>---</p> <p>-/---</p>	1-8, 12-14, 18
A		



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
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- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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Date of the actual completion of the international search

28 March 2000

Date of mailing of the international search report

05.07.00

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# INTERNATIONAL SEARCH REPORT

Internat. Application No.  
PCT/US 99/24222

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>CARMECI ET AL: "Identification of a gene (GPR30) with homology to the G-protein-coupled receptor superfamily associated with estrogen receptor expression in breast cancer" GENOMICS,US,ACADEMIC PRESS, SAN DIEGO, vol. 45, no. 3, 1 November 1997 (1997-11-01), pages 607-617-17, XP002099963 ISSN: 0888-7543</p> <p style="text-align: center;">---</p>	
A	<p>RADINSKY ET AL: "Level and function of epidermal growth factor receptor predict the metastatic potential of human colon carcinoma cells" CLINICAL CANCER RESEARCH,US,THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, vol. 1, no. 1, January 1995 (1995-01), pages 19-31-31, XP002099964 ISSN: 1078-0432</p> <p style="text-align: center;">-----</p>	

# INTERNATIONAL SEARCH REPORT

In. ational application No.  
PCT/US 99/24222

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 4  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

See additional sheets

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Invention 1: claims: 1-8, 12-14 and 18 (all partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

## 1. Invention 1: Claims: 1-8,12-14 and 18 (all partially)

An isolated and purified human protein comprising an amino acid sequence which is at least 85% identical to an amino acid sequence encoded by a nucleotide sequence consisting of SeqIdNo.1 or the complement thereof; A fusion protein comprising at least six contiguous amino acids selected from an amino acid sequence encoded by the nucleotide sequence of SeqIdNo.1 or the complement thereof; A preparation of antibodies which specifically bind to a human protein which comprises an amino acid sequence encoded by the nucleotide sequence of SeqIdNo.1 or the complement thereof; A method for detecting metastatic tumor cells in a tissue sample comprising the step of measuring in said tissue sample an expression product of a gene which comprises a coding sequence of SeqIdNo.1, wherein a tissue sample which expresses the product is categorized as containing metastatic tumor cells; A method for determining metastatic potential in a tissue sample comprising the step of measuring an expression product of a gene which comprises a sequence of SeqIdNo.1, wherein a tissue sample which expresses the product is categorized as having metastatic potential; A method of predicting the propensity for metastatic spread of a breast tumor preferentially to bone or lung comprising the step of measuring in a breast tumor sample an expression product of a gene which comprises a sequence consisting of SeqIdNo.1, wherein a breast tumor sample which expresses the product is categorized as having a propensity to metastasize to bone or lung.

## 2. Inventions 2-35: Claims: 1-8,12-14,18 and 19 (all partially, as applicable)

As for invention 1, but respectively relating to one sequence selected from the group consisting of SeqIdNo.2, 4, 5, 6, 9, 11, 13, 14, 18, 19, 20, 22, 24, 26, 27, 29, 30, 32, 33, 35, 36, 38, 39, 40, 41, 45, 48, 52, 54, 55, 57, 58, 60 and 63

## 3. Inventions 36-48: Claims: 6-8,12-14,18 and 19 (all partially, as applicable)

As for invention 1, but respectively relating to one sequence selected from the group consisting of SeqIdNo.64, 65, 66, 69, 70, 71, 72, 73, 74, 76, 80, 82 and 83.

## 4. Inventions 49: Claims: 1-5, 9-11, 15-17 (all partially)

An isolated and purified human protein comprising an amino acid sequence which is at least 85% identical to an amino acid sequence encoded by a nucleotide sequence consisting of SeqIdNo.3 or the complement thereof; A fusion protein comprising at least six contiguous amino acids selected from an amino acid sequence encoded by the nucleotide sequence of SeqIdNo.3 or the complement thereof; A preparation of antibodies which specifically bind to a human protein which comprises an amino acid sequence encoded by the nucleotide sequence of SeqIdNo.3 or the complement thereof; A method for detecting metastatic tumor cells in a tissue sample comprising the step of measuring in said tissue sample an expression product of a gene which comprises a sequence consisting of SeqIdNo.3, wherein a tissue sample which does not express the product is categorized as metastatic; A method for determining metastatic potential in a tissue sample comprising the step of measuring in a tissue sample an expression product of a gene which comprises a sequence of SeqIdNo.3, wherein a tissue sample which does not express the product is categorized as having metastatic potential

## 5. Inventions 50-75: Claims: 1-5, 9-11, 15-17 (all partially)

As for invention 49, but respectively relating to one sequence selected from the group consisting of SeqIdNo.7, 8, 10, 12, 15, 16, 17, 21, 23, 25, 28, 31, 34, 37, 42, 43, 44, 46, 47, 49, 50, 51, 53, 59, 61, 62

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

## 6. Inventions 76-84: Claims: 9-11, 15-17 (all partially)

As for invention 49, but respectively relating to one sequence selected from the group consisting of SeqIdNo.67, 68, 75, 77, 78, 79, 81, 84 and 85

## 7. Invention 85: Claim : 20 (totally) and 1-5 (all partially)

An isolated and purified human protein comprising an amino acid sequence which is at least 85% identical to an amino acid sequence encoded by a nucleotide sequence consisting of SeqIdNo.56 or the complement thereof; A fusion protein comprising at least six contiguous amino acids selected from an amino acid sequence encoded by the nucleotide sequence of SeqIdNo.56 or the complement thereof; A preparation of antibodies which specifically bind to a human protein which comprises an amino acid sequence encoded by the nucleotide sequence of SeqIdNo.56 or the complement thereof; A method of predicting propensity for metastatic spread of a colon tumor comprising the step of measuring in a colon tumor sample an expression product of a gene which comprises the nucleotide sequence shown in SeqIdNo.56, wherein a colon tumor sample which expresses the product is characterised as having a low propensity to metastasize.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 4

Claim 4, which is directed to a fusion protein which comprises a first protein segment and a second protein segment fused to each other by means of a peptide bond, wherein the first protein segment consists of at least six contiguous amino acids selected from an amino acid sequence encoded by a nucleotide sequence of SeqIdNo.1 or the complement thereof, encompasses an extremely large number of sequences. In view of that huge number, a meaningful complete search cannot be carried out. Furthermore, as none of the claimed sequences as defined in claim 4 is disclosed in the application, the Search Division is provided with no guidance to carry out at least a meaningful partial search.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.